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REMARKS

In Response to the Restriction Requirement of September 27, 2001, Applicant elected the Claims in Group I with traverse. Also, in this Response mailed December 18, 2001, Applicant cancelled Claims 12-16 and added new Claims 17-21, in order to correct a numbering error in the application as originally filed. As Applicant indicated in the Response to the Restriction Requirement, there was no Claim 12 in the application as originally filed (*i.e.*, the application was originally filed with Claims 1-11, and 13-16). Thus, Applicant submits that by canceling Claims 12-16 and adding Claims 17-21, Applicant was in compliance with 37 C.F.R. 1.126, as the original numbering of the Claims was preserved and the new Claims added in the Response to the Restriction Requirement began with the next consecutive number (*i.e.*, Claim 17). Thus, Applicant respectfully submits that the Claims as filed and indicated in the Response to the Restriction Requirement were correct. Thus, Claims 1-7, 9-11 and 17-21 were pending. However, as the Examiner has reiterated the Claim numbering objection, Applicant has amended Claims 17-21 to Claims 16-19.

Applicant appreciates the Examiner's withdrawal of the previous rejections and objections. Applicant notes that the Examiner has cited two new references against the present application (*Nakamura et al.*, and *Kunst et al.*). As these are newly cited references, with different disclosures from the references previously cited against the present application, Applicant does not understand how the previous arguments were unpersuasive in overcoming these references. Nonetheless, Applicant submits that the pending Claims are patentable over the *Nakamura et al.* and *Kunst et al.* references first cited by the Examiner in the present Final Office Action.

The Examiner argues that Claims 1-7, 9-11 and 16-19 are obvious (35 U.S.C. §103(a)) under *Nakamura et al.*, in view of *Kunst et al.* The Examiner argues that "*Nkamura et al.* . . . teach a *Bacillus subtilis* strain deficient in apr, npr and genes encoding serine proteases (page 2367, 3rd paragraph)." (Office Action, page 2).

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However, the Examiner admits that "... Nakamura et al. do not teach a microorganisms [sic] comprising a mutated or deleted gene encoding a serine protease, wherein said gene comprises SEQ ID NO:1." (Office Action, page 3). Nonetheless, the Examiner argues that "Kunst et al. ... teach a DNA molecule encoding a serine protease that is 100% identical to SEQ ID NO:2 of the instant invention ... Therefore, it would have been obvious to one having ordinary skill in the art ... to make a *Bacillus* comprising a mutated or deleted serine protease gene, apr or npr gene and to use the microorganism in production and secretion [of] heterologous enzymes without proteolytic degradation." (Office Action, page 3).

Applicant must respectfully disagree with the Examiner's arguments and rationale for the present rejection. As with the previously cited references, Applicant respectfully traverses because a *prima facie* case of obviousness is not established. As indicated previously, in order to set forth a *prima facie* case of obviousness, the Examiner must cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, and (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish **any** one of these requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicant to withdrawal of the rejection of the Claims in issue.² Applicant urges that the Examiner has failed to establish not one, but **all three** requirements, as discussed below. Furthermore, Applicant submits that the sequence of Kunst et al. is not a properly cited against the present Claims.

²See e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

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Applicant respectfully submits that the teachings of *Kunst et al.*, taken alone or in combination with *Nakamura et al.* do not teach nor even suggest the presently claimed invention. As the Examiner admits, "Nakamura et al. do not teach microorganisms comprising a mutated or deleted gene encoding a serine protease, wherein said gene comprises SEQ ID NO:1." (Office Action, page 3). This failure of *Nakamura et al.* is not remedied by the addition of the *Kunst et al.* sequence, in which a *protein sequence* is set forth. There is NO disclosure nor teaching in *Kunst et al.* of a nucleic acid sequence. Although the Examiner argues that the amino acid sequence of SEQ ID NO:2 is identical to the sequence set forth by *Kunst et al.*, the Claims recite SEQ ID NO:1, not SEQ ID NO:2. Thus, this argument does not correspond to what is actually claimed.

Indeed, Applicant respectfully submits that the present Claims are directed toward nucleic acid sequence, which is very different than amino acid sequence. As stated in *In re Bell*³,

"It may be true that, knowing the structure of the protein, one can use the genetic code to hypothesize possible structures for the corresponding gene . . . However, because of the degeneracy of the genetic code, there are a vast number of nucleotide sequences that might code for a specific protein."

Thus, Applicant respectfully submits that the *nucleic acid* sequence specifically set forth in the present Claims is neither taught nor suggested by *Kunst et al.* Furthermore, Applicant submits that the sequence disclosed by *Kunst et al.* was apparently not complete until May 30, 2000, the date indicated in the printout of the sequence record provided by the Examiner as being the date of the last sequence update. As the initial submission was apparently comprised of "preliminary partial sequence from n.a.," there is no indication that the authors were in possession of SEQ ID NO:1, as explicitly set forth in the presently pending Claims. This date is *after* the filing date of the present application.

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Thus, the sequence set forth in *Kunst et al.* cannot be treated as a prior art reference.

Furthermore, as indicated in *In re Deuel* (51 3d. 15523 (Fed. Cir. 1995)), a general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search. In addition, a general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. Even if the references provide a general motivation to search for some gene that exists (which Applicant submits they do not so motivate), SEQ ID NO:1 is not rendered obvious.

In sum, the references cited against the presently claimed invention do not teach nor suggest the elements of the Claims. Thus, Applicant submits that under the law, the present Claims are unobvious.

Applicant believes that, at best, the Examiner presents an "obvious to try" standard in determining the patentability of the present invention, a standard which has been thoroughly discredited. Indeed, an obviousness rejection is inappropriate, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 10 USPQ2d 1843, 1845 (Fed. Cir. 1989). Thus, Applicant respectfully requests that this rejection be withdrawn and the Claims be passed to allowance.

³ *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993), at 784.

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CONCLUSION

All grounds of rejection and objection of the Final Office Action of June 28, 2002, having been addressed, reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned.

Respectfully submitted,

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APPENDIX I
MARKED-UP VERSION OF SPECIFICATION'S REPLACEMENT
PARAGRAPHS AND REWRITTEN, ADDED, AND/OR CANCELLED CLAIMS

The following is a marked-up version of the Specification's replacement paragraphs pursuant to 37 C.F.R. §1.121(b), as well as a marked-up version of the Claims pursuant to 37 C.F.R. §1.121 (c)(1)(ii) with instructions and markings showing changes made herein to the previous version of record of the Specification and Claims. Underlining denotes added text while bracketing denotes deleted text.

16[17]. (Amended) The method of Claim 11 wherein said *Bacillus* cell is selected from the group consisting of *Bacillus subtilis*, *B. licheniformis*, *B. lentus*, *B. brevis*, *B. stearothermophilus*, *B. alkalophilus*, *B. amyloliquefaciens*, *B. coagulans*, *B. circulans*, *B. lautus* and *Bacillus thuringiensis*.

17 [18]. (Twice Amended) The method of Claim 17 wherein said *Bacillus* host cell further comprises a mutation or deletion in at least one of the genes encoding apr, npr, epr, wpr and mrp.

18[19]. (Twice Amended) A gram-positive microorganism having at mutation or deletion in the gene encoding serine protease 1, wherein said serine protease 1 is encoded by the nucleic acid set forth in SEQ ID NO:1.

19 [20]. (Amended) The microorganism of Claim 19 further comprising a mutation or deletion in at least one of the genes encoding apr, npr, epr, wpr and mrp.